

WHAT IS CLAIMED IS:

1. A method of characterizing a multi-determinant metabolic phenotype for at least one anticoagulant agent, wherein a plurality of phenotypic determinants are identified as corresponding to respective metabolic characteristics; said method comprising:
 - a) administering to an individual a probe substrate specific to metabolic pathway(s) for said at least one anticoagulant agent;
 - b) detecting metabolites of said metabolic pathway(s) in a biological sample from said individual in response to said probe substrate; and
 - c) characterizing respective phenotypic determinants of said multi-determinant metabolic phenotype based on detected metabolites.
2. The method of claim 1, wherein said at least one anticoagulant agent is selected from the group consisting of beta₂ Adrenoreceptor Antagonists, Neuropeptide V2 Antagonists, prostacyclin analogs, thromboxane synthase inhibitors, calcium agonists, coumarin derivatives, elastase inhibitors, Non-steroidal antiinflammatories thrombin inhibitors, lipoxygenase inhibitors, Factor VIIa inhibitors, Factor Xa inhibitors, phosphodiesterase III inhibitors, Heparins, and fibrinogen glucoprotein IIb/IIIa Antagonists.
3. The method of claim 1, wherein said at least one anticoagulant agent is warfarin.

4. The method of claim 2 which further comprises a step i) after step b):

i) quantifying a ratio of respective detected metabolites for each of said metabolic pathways in said biological sample.

5. The method of claim 4, wherein said ratio is selected from the group consisting of concentration ratio, molar ratio, chiral ratio, ratio of area under the curve and signal peak height ratio.

6. The method of claim 1, wherein said probe substrate is at least one probe substrate known to be metabolized by said metabolic pathway.

7. The method of claim 6, wherein said probe substrate is other than an inducer or inhibitor of said metabolic pathway.

8. The method of claim 1, wherein said step b) or step c) is effected using an affinity complexation agent specific to each of said metabolites.

9. The method of claim 8, wherein said affinity complexation agent is an antibody.

10. The method of claim 9, wherein said antibody is a monoclonal antibody.

11. The method of claim 9, wherein said antibody is a polyclonal antibody.

12. The method of claim 8, wherein said affinity complexation agent is a molecular imprinted polymer.

13. The method of claim 8, wherein said affinity complexation agent is an aptmer.

14. The method of claim 8, wherein said affinity complexation agent is a receptor.

15. The method of claim 8, wherein said affinity complexation agent is an anticalin.

16. The method of claim 8, further comprising a ligand binding assay.

17. The method of claim 16, wherein said ligand binding assay is selected from the group consisting of immunoassay, enzyme-linked immunosorbent assay (ELISA), microarray formatted immunoassay and microarray formatted ELISA.

18. The method of claim 16, wherein said ligand binding assay is a rapid immunoassay (Dipstick assay).

19. The method of claim 18, wherein said rapid immunoassay is based on Rapid Analyte Measurement Platform (RAMP) technology.

20. The method of claim 19, wherein said rapid immunoassay is based on light-emitting immunoassay technology.

21. The method of claim 16, wherein said ligand binding assay is performed with a biosensor.

22. The method of claim 21, wherein said biosensor is an immunosensor.

23. The method of claim 21 wherein the means of detection of said biosensor is an electrochemical sensor.

24. The method of claim 21, wherein the means of detection of said biosensor is an optical sensor.

25. The method of claim 21, wherein the means of detection of said biosensor is a microgravimetric sensor.

26. The method of claim 25, wherein said microgravimetric sensor is a quartz crystal microbalance (QCM).

27. The method of claim 1, wherein step b) is effected by using a qualitative detection instrument.

28. The method according to claim 1, wherein each of said plurality of phenotypic determinants of said multi-

determinant metabolic phenotype is an enzyme-specific determinant.

29. The method to claim 28, wherein said multi-determinant metabolic phenotype is comprised of at least one metabolic determinant indicative of an individual's metabolic capacity for at least one drug metabolizing enzyme.

30. The method of claim 29, wherein said at least one drug metabolizing enzyme is CYP2C9.

31. The method of claim 30, further comprising at least one drug metabolizing enzyme selected from the group consisting of N-acetyltransferase-1 (NAT-1), N-acetyltransferase-2 (NAT-2), CYP1A2, CYP2D6, CYP2A6, CYP2E1, CYP3A4, CYP2C19, UGTs, GSTs, and STs.

32. The method of claim 4, wherein step a) is effected by using a plurality of probe substrates and wherein each probe substrate is specific to at least one metabolic pathway of interest.

33. The method of claim 1, further comprising:

- d) measuring at least one determinant for drug clearance known to affect the toxicity or efficacy of said at least one anticoagulant agent; wherein said at least one determinant is factored together with at least rate of probe substrate metabolism to determine a non-

toxic and effective amount of said at least one anticoagulant agent to be administered to said individual.

34. The method of claim 33, wherein said at least one determinant for drug clearance is based on body surface area or hepatic enzyme levels of said individual.

35. The method of claim 1, further comprising:

d) measuring at least one determinant for drug susceptibility known to affect the toxicity or efficacy of said at least one anticoagulant agent; wherein said at least one determinant for drug susceptibility is factored together with at least rate of probe substrate metabolism to determine a non-toxic and effective amount of said at least one anticoagulant agent to be administered to said individual.

36. The method of claim 35, wherein said at least one determinant for drug susceptibility is based on pretreatment renal function of said individual determined prior to step a).

37. The method of claim 34, further comprising:

e) measuring at least one determinant for drug susceptibility known to affect the toxicity or efficacy of said at least one anticoagulant agent; wherein said at least one determinant

for drug susceptibility is factored together with at least rate of probe substrate metabolism to determine a non-toxic and effective amount of said at least one anticoagulant agent to be administered to said individual.

38. The method of claim 37, wherein said at least one determinant for drug susceptibility is based on pretreatment renal function of said individual determined prior to step a).

39. The method of claim 38, wherein said at least one anticoagulant agent is selected from the group consisting of beta₂ Adrenoreceptor Antagonists, Neuropeptide V2 Antagonists, prostacyclin analogs, thromboxane synthase inhibitors, calcium agonists, coumarin derivatives, elastase inhibitors, Non-steroidal antiinflammatories, thrombin inhibitors, lipoxygenase inhibitors, Factor VIIa inhibitors, Factor Xa inhibitors, phosphodiesterase III inhibitors, Heparins, and fibrinogen glucoprotein IIb/IIIa Antagonists.

40. The method of claim 38, wherein said at least one anticoagulant agent is warfarin.

41. The method of claim 36, wherein said at least one anticoagulant agent is selected from the group consisting of beta₂ Adrenoreceptor Antagonists, Neuropeptide V2 Antagonists, prostacyclin analogs, thromboxane synthase inhibitors, calcium agonists, coumarin derivatives,

elastase inhibitors, Non-steroidal antiinflammatories thrombin inhibitors, lipoxygenase inhibitors, Factor VIIa inhibitors, Factor Xa inhibitors, phosphodiesterase III inhibitors, Heparins, and fibrinogen glucoprotein IIb/IIIa Antagonists.

42. The method of claim 36, wherein said at least one anticoagulant agent is warfarin.

43. A method of using a multi-determinant metabolic phenotype to individualize a treatment regimen for at least one anticoagulant agent for an individual, wherein the multi-determinant metabolic phenotype of said individual is determined; a safe and therapeutically effective dose of said at least one anticoagulant agent treatment is determined and/or selected based on said multi-determinant metabolic phenotype of said individual.

44. The method of claim 43, wherein said multi-determinant metabolic phenotype is determined according to the method comprising:

- a) administering to an individual a probe substrate specific to metabolic pathway(s) for said at least one anticoagulant agent;
- b) detecting metabolites of said metabolic pathway(s) in a biological sample from said individual in response to said probe substrate; and
- c) characterizing respective phenotypic determinants of said multi-determinant

metabolic phenotype based on detected metabolites.

45. The method of claim 44, wherein said at least one anticoagulant agent is selected from the group consisting of beta₂ Adrenoreceptor Antagonists, Neuropeptide V2 Antagonists, prostacyclin analogs, thromboxane synthase inhibitors, calcium agonists, coumarin derivatives, elastase inhibitors, Non-steroidal antiinflammatories thrombin inhibitors, lipoxygenase inhibitors, Factor VIIa inhibitors, Factor Xa inhibitors, phosphodiesterase III inhibitors, Heparins; and fibrinogen glucoprotein IIb/IIIa Antagonists.

46. The method of claim 44, wherein said at least one anticoagulant agent is warfarin.

47. A method of administering to an individual at least one anticoagulant agent, said method comprising:

- a) determining a multi-determinant metabolic phenotype of said individual; and
- b) administering a safe and therapeutically effective dose of said at least one anticoagulant agent to said individual, wherein said dose has been determined based on a metabolic profile of said individual corresponding to said individual's metabolic phenotype for said at least one anticoagulant agent as represented by said multi-determinant metabolic phenotype.

48. The method of claim 47, wherein said multi-determinant metabolic phenotype is characterized according to the method comprising:

- a) administering to an individual a probe substrate specific to metabolic pathway(s) for said at least one anticoagulant agent;
- b) detecting metabolites of said metabolic pathway(s) in a biological sample from said individual in response to said probe substrate; and
- c) characterizing respective phenotypic determinants of said multi-determinant metabolic phenotype based on detected metabolites.

49. The method of claim 48, wherein said at least one anticoagulant agent is selected from the group consisting of beta₂ Adrenoreceptor Antagonists, Neuropeptide V2 Antagonists, prostacyclin analogs, thromboxane synthase inhibitors, calcium agonists, coumarin derivatives, elastase inhibitors, Non-steroidal antiinflammatories, thrombin inhibitors, lipoxygenase inhibitors, Factor VIIa inhibitors, Factor Xa inhibitors, phosphodiesterase III inhibitors, Heparins, and fibrinogen glucoprotein IIb/IIIa Antagonists.

50. The method of claim 48, wherein said at least one anticoagulant agent is warfarin.

51. An assay system for detecting the presence of enzyme-specific metabolites in a biological sample, said sample obtained from an individual treated with a known amount of at least one probe substrate for at least one anticoagulant agent, specific for metabolic pathways of said metabolites, said assay comprising:

- a) means for receiving said biological sample, including a plurality of affinity complexation agents contained therein;
- b) means for detecting presence of said enzyme-specific metabolites bound to said affinity complexation agents; and
- c) means for quantifying ratios of said metabolites to provide corresponding phenotypic determinants;

wherein said phenotypic determinants provide a metabolic phenotypic profile of said individual.

52. The assay system of claim 51, wherein said at least one anticoagulant agent is selected from the group consisting of beta₂ Adrenoreceptor Antagonists, Neuropeptide V₂ Antagonists, prostacyclin analogs, thromboxane synthase inhibitors, calcium agonists, coumarin derivatives, elastase inhibitors, Non-steroidal antiinflammatories thrombin inhibitors, lipoxygenase inhibitors, Factor VIIa inhibitors, Factor Xa inhibitors, phosphodiesterase III inhibitors, Heparins, and fibrinogen glucoprotein IIb/IIIa Antagonists.

53. The assay system of claim 51, wherein said at least one anticoagulant agent is warfarin.

54. The assay system of claim 52, wherein said step b) or step c) is effected according to the method comprising:

- a) administering to an individual a probe substrate specific to metabolic pathway(s) for said at least one anticoagulant agent;
- b) detecting metabolites of said metabolic pathway(s) in a biological sample from said individual in response to said probe substrate; and
- c) characterizing respective phenotypic determinants of said multi-determinant metabolic phenotype based on detected metabolites;

wherein said probe substrate is at least one substrate known to be metabolized by said metabolic pathway, and wherein said probe substrate is other than an inducer or inhibitor of said metabolic pathway.

55. The assay system of claim 54, wherein said assay is a ligand binding assay.

56. The assay system of claim 55, wherein said ligand binding assay is selected from the group consisting of immunoassay, enzyme-linked immunosorbent assay (ELISA), microarray formatted immunoassay and microarray formatted ELISA.

57. The assay system of claim 56, wherein said means for receiving said biological sample is a multi-well microplate including said plurality of affinity complexation agents in each well.

58. The assay system of claim 57, wherein said plurality of affinity complexation agents are bound to each well in an array-based format.

59. The assay system of claim 58, wherein said means for detecting said presence of said metabolites bound to said binding agents is a charge-coupled device (CCD) imager.

60. The assay system of claim 59, wherein said means for said quantifying ratios of said metabolites is a densitometer.

61. A method of using an enzyme-specific assay for the individualization of treatment with at least one anticoagulant agent, said method comprising:

- a) conducting said assay to identify phenotypic determinants in a biological sample obtained from an individual treated with a probe substrate for said at least one anticoagulant agent;
- b) determining a rate of drug metabolism according to said determinants; and

c) determining and/or selecting a safe and therapeutically effective dose of said class of Anticoagulants compounds for said individual based on said rate.

62. The method of claim 61, wherein said assay comprises:

- a) means for receiving said biological sample, including a plurality of affinity complexation agents contained therein;
- b) means for detecting presence of said enzyme-specific metabolites bound to said affinity complexation agents; and
- c) means for quantifying ratios of said metabolites to provide corresponding phenotypic determinants;

wherein said phenotypic determinants provide a metabolic phenotypic profile of said individual.

63. The method of claim 62, wherein said at least one anticoagulant agent is selected from the group consisting of beta2 Adrenoreceptor Antagonists, Neuropeptide V2 Antagonists, prostacyclin analogs, thromboxane synthase inhibitors, calcium agonists, coumarin derivatives, elastase inhibitors, Non-steroidal antiinflammatories thrombin inhibitors, lipoxygenase inhibitors, Factor VIIa inhibitors, Factor Xa inhibitors, phosphodiesterase III inhibitors, Heparins, and fibrinogen glucoprotein IIb/IIIa Antagonists.

64. The method of claim 63, wherein said at least one anticoagulant agent is warfarin.

65. The method of claim 63, wherein said enzyme-specific assay is selected from the group consisting of immunoassay, enzyme-linked immunosorbent assay (ELISA), microarray formatted immunoassay and microarray formatted ELISA.

66. The method of claim 65, wherein said rate of drug metabolism corresponds to a ratio of phenotypic determinants, wherein said phenotypic determinants are enzyme-specific determinants.

67. The method of claim 66, wherein said ratio is selected from the group consisting of concentration ratio, molar ratio, chiral ratio, ratio of area under the curve and signal peak height ratio.

68. The method of claim 67, wherein said phenotypic determinants comprise phenotypic determinants for CYP2C9.

69. The method of claim 68, wherein said phenotypic determinants further comprise phenotypic determinants for any one or more of N-acetyltransferase-1 (NAT1), N-acetyltransferase-2 (NAT2), CYP1A2, CYP2A6, CYP2D6, CYP2E1, CYP3A4, and CYP2C19, UGTs, GSTs, and STs.

70. A method of screening a plurality of individuals for participation in a drug treatment trial assessing the therapeutic effect of at least one anticoagulant agent, said method comprising:

- a) selecting individuals having a metabolic phenotype characterized as effective for metabolizing said at least one anticoagulant agent.

71. The method of claim 70 wherein said multi-determinant metabolic phenotype is determined according to the method comprising:

- a) administering to an individual a probe substrate specific to metabolic pathway(s) for said at least one anticoagulant agent;
- b) detecting metabolites of said metabolic pathway(s) in a biological sample from said individual in response to said probe substrate; and
- c) characterizing respective phenotypic determinants of said multi-determinant metabolic phenotype based on detected metabolites.

72. The method of claim 71, wherein said at least one anticoagulant agent is selected from the group consisting of beta2 Adrenoreceptor Antagonists, Neuropeptide V2 Antagonists, prostacyclin analogs, thromboxane synthase inhibitors, calcium agonists, coumarin derivatives, elastase inhibitors, Non-steroidal antiinflammatories thrombin inhibitors, lipoxygenase inhibitors, Factor VIIa inhibitors, Factor Xa inhibitors, phosphodiesterase III inhibitors, Heparins, and fibrinogen glucoprotein IIb/IIIa Antagonists.

73. The method of claim 72, wherein said at least one anticoagulant agent is warfarin.

74. A method of screening a plurality of individuals for treatment with at least one anticoagulant agent, said method comprising:

- a) genotyping said individuals to identify individuals lacking at least one allelic variation known to prompt toxicity of said at least one anticoagulant agent; and
- b) selecting individuals having a metabolic phenotype characterized as effective for metabolizing said at least one anticoagulant agent..

75. The method of claim 74 further comprising determining a safe and therapeutically effective amount of said at least one anticoagulant agent to be administered to each of said individuals lacking said at least one allelic variation, said effective amount corresponding to an individual-specific rate of drug metabolism as determined by phenotypic determinants specific for at least one enzyme known to metabolize said at least one anticoagulant agent.

76. The method of claim 75, wherein said step of characterizing a metabolic phenotype comprises a ligand-binding assay specific for said at least one enzyme known to metabolize said at least one anticoagulant agent.

77. The method of claim 76, wherein said at least one anticoagulant agent is selected from the group consisting of beta₂ Adrenoreceptor Antagonists, Neuropeptide V2 Antagonists, prostacyclin analogs, thromboxane synthase inhibitors, calcium agonists, coumarin derivatives, elastase inhibitors, Non-steroidal antiinflammatories thrombin inhibitors, lipoxygenase inhibitors, Factor VIIa inhibitors, Factor Xa inhibitors, phosphodiesterase III inhibitors, Heparins, and fibrinogen glucoprotein IIb/IIIa Antagonists.

78. The method of claim 77, wherein said at least one anticoagulant agent is warfarin.

79. The method of claim 77, wherein said ligand-binding assay is selected from the group consisting of immunoassay, enzyme-linked immunosorbent assay (ELISA), microarray formatted immunoassay and microarray formatted ELISA.

80. The method of claim 79, wherein said rate of drug metabolism corresponds to a ratio of phenotypic determinants for at least CYP2C9 enzyme.

81. The method of claim 80, wherein said ratio is selected from the group consisting of concentration ratio, molar ratio, chiral ratio, ratio of area under the curve and signal peak height ratio.

82. The method of claim 81, wherein said ligand-binding assay further provides means to determine phenotypic determinants for at least one of the following

enzymes: NAT2, CYP1A2, NAT1, CYP2A6, CYP2D6, CYP2E1, CYP3A4, CYP2C19, UGTs, GSTs, and STs.

83. A method of screening a plurality of individuals for participation in a drug treatment trial assessing the therapeutic effect of a candidate anticoagulant agent treatment, said method comprising:

- a) genotyping each of said individuals to identify individuals lacking at least one allelic variation known to prompt the toxicity of said anticoagulant agent; and
- b) characterizing a multi-determinant metabolic phenotype of said identified individuals of step a) to determine each individual's ability to metabolize said anticoagulant agent.

84. The method of claim 83, wherein said at least one anticoagulant agent is selected from the group consisting of beta₂ Adrenoreceptor Antagonists, Neuropeptide V2 Antagonists, prostacyclin analogs, thromboxane synthase inhibitors, calcium agonists, coumarin derivatives, elastase inhibitors, Non-steroidal antiinflammatories thrombin inhibitors, lipoxygenase inhibitors, Factor VIIa inhibitors, Factor Xa inhibitors, phosphodiesterase III inhibitors, Heparins, and fibrinogen glucoprotein IIb/IIIa Antagonists.

85. The method of claim 84, wherein said at least one anticoagulant agent is warfarin.

86. The method of claim 84, wherein said multi-determinant metabolic phenotype is comprised of at least one determinant indicative of an individual's metabolic capacity for at least one drug metabolizing enzyme.

87. The method of claim 86, wherein said at least one drug metabolizing enzyme is selected from the group consisting of N-acetyltransferase-1 (NAT1), N-acetyltransferase-2 (NAT2), CYP1A2, CYP2A6, CYP2D6, CYP2E1, CYP3A4, CYP2C9, CYP2C19, UGTs, GSTs, and ST.

88. The method of claim 87, wherein said rate of drug metabolism corresponds to a ratio of said phenotypic determinants for said at least one enzyme.

89. The method of claim 88, wherein said ratio is selected from the group consisting of concentration ratio, molar ratio, chiral ratio, ratio of area under the curve and signal peak height ratio.

90. The method of claim 4, wherein said step b) or step c) is effected using an affinity complexation agent specific to each of said metabolites.

91. The method of claim 1, wherein said step b) and step c) are effected using an affinity complexation agent specific to each of said metabolites.

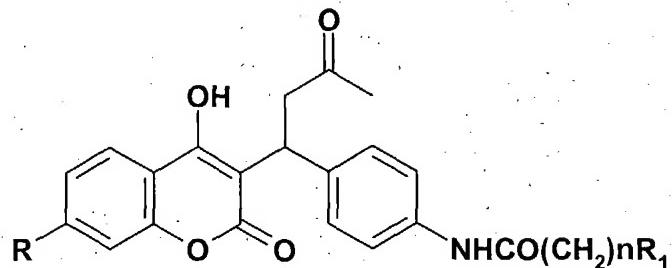
92. The method of claim 4, wherein said step b) and step c) are effected using an affinity complexation agent specific to each of said metabolites.

93. The assay system of claim 51, wherein said step b) and step c) is effected according to the method comprising:

- a) administering to an individual a probe substrate specific to metabolic pathway(s) for said at least one anticoagulant agent;
- b) detecting metabolites of said metabolic pathway(s) in a biological sample from said individual in response to said probe substrate; and
- c) characterizing respective phenotypic determinants of said multi-determinant metabolic phenotype based on detected metabolites;

wherein said probe substrate is at least one substrate known to be metabolized by said metabolic pathway, and wherein said probe substrate is other than an inducer or inhibitor of said metabolic pathway.

94. Compounds having formula V:



wherein, n = 1-8, R = H, or OH and R₁ is selected from the group consisting of CO₂H, OH, NH₂ and CH₂X, wherein X = a halogen.

95. Compounds of claim 94, wherein said compounds are R-chiral form.

96. Compounds of claim 94, wherein said compounds are S-chiral form.

97. An immunogenic composition for raising antibodies specific to warfarin in a subject, which comprises a compound of claim 95 modified with an immunogenic moiety or carrier in association with a pharmaceutically acceptable carrier.

98. An immunogenic composition for raising antibodies specific to warfarin in a subject, which comprises a compound of claim 96 modified with an immunogenic moiety or carrier in association with a pharmaceutically acceptable carrier.

99. The immunogenic composition of claim 97, wherein said subject is an animal selected from the group consisting of mammals and birds.

100. The immunogenic composition of claim 98, wherein said subject is an animal selected from the group consisting of mammals and birds.

101. The immunogenic composition of claim 99, wherein said animal is a rabbit.

102. The immunogenic composition of claim 100, wherein said animal is a rabbit.

103. The immunogenic composition of claim 97, wherein said immunogenic moiety or carrier is selected from the group consisting of keyhole limpet hemocyanin (KLH) and bovine serum albumin (BSA).

104. The immunogenic composition of claim 98, wherein said immunogenic moiety or carrier is selected from the group consisting of keyhole limpet hemocyanin (KLH) and bovine serum albumin (BSA).

105. A method of raising antibodies which bind to warfarin, which comprises administering an immunogenic amount of an immunogenic composition of claim 97 to an animal.

106. A method of raising antibodies which bind to warfarin, which comprises administering an immunogenic amount of an immunogenic composition of claim 98 to an animal.

107. A method of producing antibodies which bind to warfarin, comprising: a) treating an animal with an immunogenic amount of an immunogenic composition of claim 97 to produce antibodies; and b) isolating said antibodies of step a) from serum of said animal.

108. A method of producing antibodies which bind to warfarin, comprising: a) treating an animal with an immunogenic amount of an immunogenic composition of claim

98 to produce antibodies; and b) isolating said antibodies of step a) from serum of said animal.

109. An isolated antibody or antigen binding fragment thereof, which binds to a compound of claim 95.

110. An isolated antibody or antigen binding fragment thereof, which binds to a compound of claim 96.

111. An isolated antibody or antigen binding fragment thereof according to claim 109, wherein said antibody is a monoclonal antibody or a polyclonal antibody.

112. An isolated antibody or antigen binding fragment thereof according to claim 110, wherein said antibody is a monoclonal antibody or a polyclonal antibody.

113. An isolated antibody or antigen binding fragment thereof according to claim 111, wherein said binding fragment is selected from the group consisting of a Fab fragment, a $F(ab')_2$ fragment and a Fv fragment.

114. An isolated antibody or antigen binding fragment thereof according to claim 112, wherein said binding fragment is selected from the group consisting of a Fab fragment, a $F(ab')_2$ fragment and a Fv fragment.

115. A hybridoma cell line that produces a monoclonal antibody which binds to a compound according to claim 95.

116. A hybridoma cell line that produces a monoclonal antibody which binds to a compound according to claim 96.

117. The method of claim 9, wherein said antibody binds to a compound according to claim 95.

118. The method of claim 9, wherein said antibody binds to a compound according to claim 96.

119. The method of claim 9, wherein said antibody is an antibody according to claim 109.

120. The method of claim 9, wherein said antibody is an antibody according to claim 110.

121. An assay kit for detecting the presence of enzyme-specific metabolites in a biological sample, said sample obtained from an individual treated with a known amount of at least one probe substrate for at least one anticoagulant agent, which comprises at least two antibodies each specific to said at least one probe substrate or a different metabolite of said at least one probe substrate to measure their molar ratio in a biological sample of an individual after being treated with said at least one probe substrate, wherein said at least one antibody is an antibody according to claim 109 or claim 110.

122. The assay kit of claim 121, wherein said at least one anticoagulant agent is selected from the group consisting of beta₂ Adrenoreceptor Antagonists, Neuropeptide V2 Antagonists, prostacyclin analogs, thromboxane synthase inhibitors, calcium agonists, coumarin derivatives, elastase inhibitors, Non-steroidal antiinflammatories thrombin inhibitors, lipoxygenase

inhibitors, Factor VIIa inhibitors, Factor Xa inhibitors, phosphodiesterase III inhibitors, Heparins, and fibrinogen glucoprotein IIb/IIIa Antagonists.

123. The assay kit of claim 121, wherein said at least one anticoagulant agent is warfarin.